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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,748	06/18/2001	Kunio Shiota	04853.0074	8762

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EXAMINER

BRUSCA, JOHN S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 02/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/881,748

Applicant(s)

SHIOTA ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-18 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5-13 and 15-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/02, 5/04, 12/04, 1/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 December 2004 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 10-13, 15, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 10-13, 15, and 16 are indefinite for recitation in claim 1, lines 8-12 of the phrase "the cell-, tissue-, or nucleus-specific DNA methylation pattern" because it is not clear if the pattern referred to is the pattern of the test cell or the known cell.

The rejection would be overcome by amending claim 1 to add the phrase "of the known cell" to the above phrase.

For the purpose of examination, the claims have been assumed to incorporate the suggested amendments.

Claim Rejections - 35 USC § 102

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4. The rejection of claims 1, 5, 7, and 11 under 35 U.S.C. 102(b) as being anticipated by Duffy in the Office action mailed 24 December 2003 is withdrawn in view of the applicant's amendment to the claims and arguments on page 10 of their response filed 22 December 2004 that Duffy does not show detection of methylation patterns of CpG sequences.

5. The rejection of claims 1, 5-7, 9-11, and 13 under 35 U.S.C. 102(b) as being anticipated by Zhu et al. in the Office action mailed 24 December 2003 is withdrawn in view of the applicant's amendment to the claims and arguments on page 15 of their response filed 22 December 2004 that Zhu et al. does not show matching of methylation patterns of a test cell and a known cell.

6. The rejection of claims 1, 5, 7, 8, 11, and 12 under 35 U.S.C. 102(b) as being anticipated by Hertz et al. in the Office action mailed 24 December 2003 is withdrawn in view of the applicant's amendment to the claims and arguments on page 16 of their response filed 22 December 2004 that Hertz et al. does not show matching of methylation patterns of a test cell and a known cell.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an

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international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Olek et al. (U.S. Patent No. 6,214,556).

The claims are drawn to a method of comparison of DNA methylation patterns of a test cell and a known cell to assay for identity of the two cell types. In some embodiments at least 1,000 gene regions are examined.

Olek et al. shows in the abstract and throughout a method of comparing methylation fingerprint patterns of different cells to classify a test cell. Olek et al. shows in column 14, lines 50-58 and column 17, lines 30-40 that thousands or millions of methylcytosine locations are assayed to form the fingerprints. Olek et al. details in columns 24-25 methods of comparison of methylation fingerprints of different cells to classify cells.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 5-7, 9, 11, 13, and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olek et al. in view of Ohgane et al. (cited in the Information Disclosure Statement filed 24 May 2004).

The claims are drawn to a method of comparison of DNA methylation patterns of a test cell and a known cell to assay for identity of the two cell types. In some embodiments a differentiation-state specific methylation pattern is compared, at least 1,000 methylation sites are compared, the nucleotide sequence of a methylation site is determined, or the methylation pattern is determined by the RLGS method.

Olek et al. shows in the abstract and throughout a method of comparing methylation fingerprint patterns of different cells to classify a test cell. Olek et al. shows in column 14, lines 50-58 and column 17, lines 30-40 that thousands or millions of methylcytosine locations are assayed to form the fingerprints. Olek et al. details in columns 24-25 methods of comparison of methylation fingerprints of different cells to classify cells. Olek et al. does not explicitly show

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comparison of cells of different differentiation states, determination of the nucleotide sequence of a region comprising a methylation site, or determining methylation sites by use of the RLGS method.

Ohgane et al. shows in the abstract and throughout, and especially in Figure 1 and Tables 1-3 comparison of methylation patterns at 2900 sites of polyploidy rat trophoblast giant cell DNA with that of diploid labyrinth zone and maternal kidney cells by use of the RLGS method. Four regions were sequenced to analyze the sequence of CpG islands in the methylated regions. Ohgane et al. conclude that cells of different differentiation states in the placenta have different methylation patterns.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the identification method of Olek et al. to identify differentiation states of cells because Ohgane et al. shows that differentiation states correlate with different methylation patterns. It would have been further obvious to use the RLGS method to determine methylation patterns because Ohgane et al. shows that the RLGS method allows for determination of thousands of sites of methylation. It would have been further obvious to sequence genomic DNA from methylation sites to analyze the types of sequences that are methylated, such as CpG islands, as shown by Ohgane et al.

13. Claims 1, 5, 8, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olek et al. in view of Ohgane et al. as applied to claims 1, 5-7, 9, 11, 13, and 15-18 above, and further in view of Onno et al.

The claims are drawn to a method of identification of stem cells by comparison of methylation patterns.

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Olek et al. in view of Ohgane et al. as applied to claims 1, 5-7, 9, 11, 13, and 15-18 above does not show identification of stem cells.

Onno et al. shows in the abstract and Table 1 that CD34+ hematopoietic stem cells have a different methylation pattern than CD2+ lymphocytes.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the identification method of Olek et al. in view of Ohgane et al. as applied to claims 1, 5-7, 9, 11, 13, and 15-18 above to identify stem cells because Onno et al. shows that stem cells have characteristic methylation patterns that allow for their identification by determination of methylation fingerprints.

Conclusion

14. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also

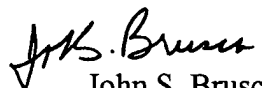
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enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 10 February 2005

John S. Brusca
Primary Examiner
Art Unit 1631

jsb